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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/217,324	03/24/94	OSBORNE	W 163363

HM12/0203
TOWNSEND AND TOWNSEND AND CREW
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EXAMINER	
CLARK, D	
ART UNIT	**PAPER NUMBER**
1633	26

DATE MAILED: 02/03/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/217,324	Osborne et al.
Examiner	**Group Art Unit**
Deborah Clark	1633

☒ Responsive to communication(s) filed on *Jan 12, 2000* .

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-22* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-22* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 08/24/99 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/217,324 is now acceptable, based upon the response to the letter mailed 09/07/99 which was received 01/12/00, a CPA has been established. An action on the CPA follows.

2. No amendment has been received.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

4. Claims 11-22 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims stand rejected for reasons of record.

In the communication filed 02/11/97 applicants argue that the rejection of record fails to provide specific and sufficient evidence supporting the opinion that the claims are not enabled by

the specification. These arguments are not deemed persuasive. The previous office actions clearly addressed the high level of unpredictability in the art of gene therapy. The fact that no narrow and specific reference has been offered to profess the high level of unpredictability in the art with regards to applicants specific invention does not take away from the fact that the level of unpredictability in the art at the time the invention was made was such that undue experimentation be required to practice the claimed invention. It is well known in the art that while some progress has been made toward human gene therapy, only a handful of clinical trials and very limited success have been reported to date. With respect to a prima facie case of nonenablement, while a single embodiment may provide broad enablement in cases involving predictable factors, in cases involving unpredictable factors, such as physiological activity, a further showing is required. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970).

It is therefore concluded that in light of the quantity of experimentation necessary, the lack of adequate direction or guidance presented, the lack of correlatable working examples, the nature of the invention, the state of the prior art with its recognized unpredictability, and the breadth of the claims, it would require undue experimentation for others skilled in the art to practice the invention.

Claim Rejections - 35 USC § 103

5. Claims 1-10 stand rejected under 35 USC 103 as being unpatentable over Zalewski et al. (WO 93/15609) taken with Nabel et al. (U.S. 5,328,470) and Anderson et al. (WO 90/224,525).

In the response filed 02/11/97 applicants argue that the Zalewski et al. reference fails to adequately suggest the claimed invention as it relates only to injection and catheter-based implant devices. These arguments are not deemed persuasive as the rejection in the previous action was made as a result of properly combining the prior art to arrive at applicants' invention with both motivation to do so and a substantial expectation of success. The fact that the Zalewski et al. reference does not specifically disclose an implantable prosthetic device lined with SMC (smooth muscle cells) does not take away from the fact that the Nabel reference does. Moreover, Anderson et al. also discloses to the skilled artisan a vascular graft coated with genetically modified autologous endothelial cells , and further discloses the use of this invention to deliver erythropoietin, Factor IX, G-CSF and GM-CSF proteins, among others.

The Nabel reference discloses the in situ transduction of endothelial and smooth muscle cells of the arterial wall or the deposition of cells transduced *ex vivo*, using the catheter to deposit the cells or appropriate gene transfer vehicle (pages 68, see "II: Introduction of cells expressing normal or exogenous proteins into the vasculature "). Nabel discloses the use of the invention to deliver insulin (page 5, line 30), or anticoagulant factors such as urokinase (page 11, lines 46-49). Nabel thus discloses in situ gene transduction of smooth muscle cells for therapeutic benefit, but

does not disclose a vascular graft containing transduced smooth muscle cells as the method of delivering the gene product of interest.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a synthetic vascular graft to transplant endothelial and smooth muscle cells into a blood vessel and to substitute genetically modified cells for unmodified cells, based on the teachings of the Nabel reference to genetically modify cells of the arterial wall for therapeutic purposes. Therefore, absent any unexpected results, the invention is considered *prima facie* obvious over the prior art of record. In order to establish unexpected results for a claimed invention, the objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support. In re Boesch, 617 F.2d 272, 205 USPQ 215 (CCPA 1980); In re Greenfield, 571 F.2d 1185, 197 USPQ 227 (CCPA 1978); In re Tiffin, 443 F.2d 394, 170 USPQ 88 (CCPA 1971).

Conclusion

6. No claim is allowed.

7. All claims are drawn to the same invention claimed in the parent application prior to the filing of this Continued Prosecution Application under 37 CFR 1.53(d) and could have been finally rejected on the grounds and art of record in the next Office action. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing under 37

CFR 1.53(d). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Clark whose telephone number is (703) 305-4051. The examiner can normally be reached on Mondays-Fridays from 7:10 a.m. EST to 3:40 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Deborah Clark

DEBORAH J. CLARK
PATENT EXAMINER